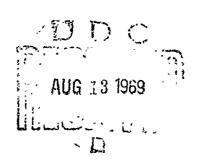
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A FURTHER SURVEY OF COMPOUNDS FOR RADIATION PROTECTION

VIVIAN PLZAK, M.S. JOHN DOULL, Ph. D., M.D.

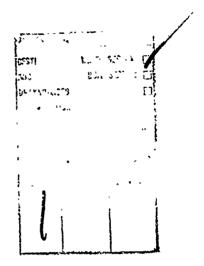




USAF School of Aerospace Medicine Aerospace Medical Division (AFSC) Brooks Air Force Base, Texas

February 1969

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A FURTHER SURVEY OF COMPOUNDS FOR RADIATION PROTECTION

VIVIAN PLZAK, M.S. JOHN DOULL, Ph. D., M.D.

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FOREWORD

This report was prepared at the USAF Radiation Laboratory of the University of Chicago and represents a summary of unpublished data. It is a sequel to "A Survey of Compounds for Radiation Protection" published in April 1962 as SAM-TR-62-29 by the USAF School of Aerospace Medicine. This compilation includes work accomplished from January 1961 through April 1965 under task No. 775703 and contract No. 41(609)-2977. The contract monitor was Lieutenant Colonel George S. Melville, Jr., Radiobiology Division, USAF School of Aerospace Medicine. The report was received for publication on 1 November 1968.

The animals involved in this study were maintained in accordance with the "Guide for Laboratory Animal Facilities and Care" as published by the National Academy of Sciences-National Research Council.

This report has been reviewed and is approved.

GEORGE E. SCHAFER

Colonel, USAF, MC

Commander

ABSTRACT

This report summarizes the results obtained with 617 compounds tested for their radioprotective activity in adult male mice irradiated with a control-demonstrated LD $_{99}$, of 800 R (250 kyp) x-rays. A compound was considered to exhibit radioprotective activity if it (1) permitted any of the treated mice to survive for 30 days after the otherwise lethal whole-body x-irradiation or (2) increased the median survival time of treated animals by 5 days or more beyond the median urvival time of the untreated control mice (9 \pm 3 days).

Of the 617 compounds tested, 245 successfully passed one or both of the stated specifications. Additionally, data are offered to allow comparisons of chemically related groups for structure-activity relationships, and to indicate the types of structures which offer the greatest promise as a source of more effective and less toxic radioprotective agents.

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A FURTHER SURVEY OF COMPOUNDS FOR RADIATION PROTECTION

I. INTRODUCTION

The purpose of the radiation screening program of the University of Chicago was to find chemical or biologic agents which exhibited prophyractic or therapeutic effectiveness against radia on injury. Testing the ability of such agents o prolong survival or to reduce lethality in x-ir adiated mice was one phase of our efforts to find practical methods to modify radiation injury in animals. Other phases of the program included: (1) the inventigation of the physiologic and biochemical mechanisms responsible for the toxic and protective effects of radioprotective agents in mice and other species; (2) the evaluation of the efficacy of such agents against chronic radiation exposure and against exposure to other types of ionizing radiation; and (3) the ability of various environmental and pharmacologic factors to modify either the toxic or the protective properties of single agents or of combinations of racioprotective agents.

A previous survey of approximately 1,200 compounds was published in April 1962. The present report summarizes the results that were obtained with approximately 600 compounds tested from January 1961 through April 1965. It has a twofold purpose: (1) to facilitate the comparison of chemically related groups for structure activity relationships, and (2) to indicate the types of structures which offer the greatest promise as a source of more effective and less toxic radioprotective agents. Initially, the compounds used in the testing program were selected with the idea of obtaining examples of as many different chemical types as possible. Since more information has

been accumulated on potentially radioprotective agents of a rather large number of chemical types, it is now possible to depend less on the survey approach of selection and more on trying to obtain compounds designed to provide more specific data on the structure-activity relationships within each chemical type.

II. EXPERIMENTAL METHODS

Adult male mice (6 to 8 weeks old) from Carworth Farms (CF₁) were used in the studies. The average weight was from 20 to 25 gm. The mice were housed in an air-conditioned room (75° to 80° F.) and were provided with Rockland mouse pellets and water ad libitum. Both control and treated animals were selected at random from a single shipment so that their age and physical condition would be comparable. All the mice were kept under observation for at least one week before they were used. Those that appeared to be unhealthy or failed to gain weight at a normal rate were removed for autopsy.

To evaluate the radioprotective activity of the compounds, the mice were divided into groups of 10 and injected intraperitoneally 10 to 15 minutes prior to the administration of a lethal (800 R) dose of whole-body x-irradiation. Each compound was tested for protective effects at two or more dosage levels, one of which was close to the maximum tolerated dosage level for that particular compound. Distilled water was used as the vehicle whenever possible and the concentration of the solution was adjusted so that no animal received more than 2% of its body weight with each injection.

When necessary, the pH was adjusted to approximately 7.0 with either 18° HCl or 18 NaOH. Compounds which were insoluble in water or in propylene glycol (PG) were dissolved in cottonseed oil or suspended in a 0.5% solution of carboxymethylcellulose. Control animals were injected with a comparable amount of the vehicle used to prepare the solution and were irradiated simultaneously with the treated groups. The loss of weight and the mortality in both groups were recorded daily for 30 days after the x-ray exposure or until all of the mice were dead.

The radiation exposures were given as single whole-body 250 kvp, 15 ma. x-ray exposures using either a G.E. Maximar or a Keleket x-ray therapy unit. The added filtration consisted of 0.25 mm. of copper and 1.0 mm. of aluminum, and the target-skin distance was 75 cm. The dose rate in air was determined prior to each radiation period, by use of Victoreen ionization thimbles (100 R); it was found to average between 40 and 43 R per minute. The mice were placed in individual plastic tubes (50-ml. centrifuge tubes provided with numerous air holes) which, in turn, were positioned radially on a rotating turntable to equalize the dose of x-ray. The environmental temperature was maintained at 75°F, during the irradiation period to minimize the effect of variations in the environmental stress in both the control and treated groups.

HI. RESULTS

Preliminary toxicity tests were conducted for each compound before the radiation studies to ascertain the maximum tolerated dose which could be given the animals without causing drug lethality. For these studies, small groups of mice were injected intraperitoneally with increasing dosage levels of each compound and the mortality observed for a week. The approximate LD₅₀ (7 days) thus obtained was used as a basis for selecting the dosage levels to be used for the radiation studies.

Doses exceeding 1,000 mg. kg. were not used, since the limited size of the sample and the disad an ages of injecting an increased

amount of vehicle made the larger doses impractical. The approximate LD_{.0} in milligrams per kilogram for each of the compounds tested is included in the tables which comprise the remaining part of this report.

The x-ray dosage level employed (800 R) uniformly caused a mortality greater than 99% within two weeks after the exposure under our experimental conditions. Radiation deaths usually began on the fifth or sixth day after the x-ray exposure and the median survival time (ST₅₀) of untreated animals was 9 ± 3 days. A compound was considered to exhibit radioprotective activity if it increased the median survival time by 5 days or more, or if it permitted any of the treated animals to survive for 30 days after the otherwise lethal whole-body x-irradiation.

Since all of these studies were carried out by use of a single dose of x-irradiation (800 R), the results do not provide a precise quantitation of the radioprotective effect of each compound tested. However, the protective effect or dose reduction factor (DRF) resulting from the preirradiation administration of a compound can be estimated on the basis of the x-ray dosage level which would be required to produce a comparable mortality at 30 days after the irradiation exposure. The LD₅₀ (30-day) value for the adult CF_1 male mice used in these studies was 542 ± 18 R. The estimated DRF values are given in table I.

TABLE I

Estimated dose reduction factors based on 30-day mortality data

Percent %rvival*	DRF†
10 to 20	1.3
30 to 40	1.4
50 to 60	1.5
70 to 80	1.6
90 to 100	1.7

^{*}Percent of treated animals (overlap at $|\psi\rangle$ days after 800 R x-translation.

[†] Admir stered radiation dose disided by effective rightion dose.

In the tables which comprise the remaining part of the report the compounds are listed in order of increasing complexity within each of the chemical types. The name of each compound is listed with the vehicle used. In the radiation studies the change in ST_{50} indicates

the increase or decrease (in days) of the median survival time of the treated animals when compared to that of the simultaneously irradiated control (vehicle only) groups.

¹The symbol representing vehicle (e.g., HOH) appears in parentheses below the name of the compound.

ALCOHOLS AND THIOLS

Compound and vehicle used for toxicity and radiation tests	Toxicity	Kadiation studies		
	Approx. LD ₅₀ (mg./kg.)	Dose (mg./kg.)	Change in ST ₅₀ (days)	Mortality at 30 days
2-Methylaminoethanol	250	200	-4	10/10
(HOH)		100	0	10/10
1-Amino-2-propanol	400	300	-10	10/10
(HOH)		100	-4	10/10
Acetone sodium bisulfite	> 1000	1000	+2	10/10
(HOH)		500	3	10/10
Glyoxal (30% in water)	750	500	-5	9/10
(HOH)		300	+3	5/10
Propylene glycol (1,2-propanediol) (100%)	17500	3000 5000 6250 7500 8750 10000 12500	+2 0 +2 -3 -4 -3 -7	10/10 8/10 9/10 10/10 10/10 10/10 10/10
2-Isobutylaminoethanol	250	200	-3	10/10
(HOH)		100	-2	10/10
2,3-Butanediol	> 1000	1000	-1	10/10
(HOH)		500	-2	10/10
Batyl alcohol	750	500	-1	10/10
(PG)		250	-2	10/10
3-(N-Methylisopropylamino)-3-methyl-2-	250	200	0	10/10
butanol hydrochloride		100	-5	10/10
(HOH)		50	-8	10/10
Calcium gluconate (HOH)		10	0	10/10
2-Amino-1-phenyl-1-ethanol	250	200	-5	10/10
(HOH)		100	-9	10/10
2,6-Dimethylphenol (PG)	150	100 50	0 -1	10/10 10/10
2,4-Di-tert-butylphenol	25	10	-3	10/10
(PG)		5	-2	10/10
N-Propyl-p-hydroxybenzoate (PG)	200	100	-1 0	10/10 10/10

Sodium-p-hydroxyphenylarsonate	1000	500	-6	10/10
(HOH)		200	+2	10/10
o-Methoxyphenol	250	200	-4	9 10
(PG)		100	0	10/10
P-Methoxy-4-n-pr py phenol (PG)	150	100 50	-9 +2	10 10 7/10
n-Chloroacetylcatechol	75	50	-6	16-10
(HOH)		25	+6	10/10
Pyrogaliol	400	300	-3	10/10
(HOH)		100	+2	10/10
Desoxypyridoxine hydrochloride	150	100	-5	10/10
(HOH)		50	0	10/10
-Aminophenol	200	100	-1	10 10
(PG)		50	0	10/10
n-Aminophenol	150	100	€	10/10
(PG)		50	-1	10/10
p-Nitrophenol (PG)	75	50 25 10	-2 -2 -2	10/10 10/10 10/10
o-Aminophenol hydrochloride	750	500	2	10 10
(HOH)		300	4	10/10
l-Amino-3-methylphenol	200	100	-1	10/10
(PG)		50	-2	10/10
p-Phenylpheno!	150	100	-2	10 10
(PG)		50	0	10/10
p-Hydroxydiphenyl (PG)	150	100 50	0	10 · 10 10/10
Naphthoresorcinol (PG)	200	100 50	0 0	8/10 10/10
o,o'-Biphenol	150	100	-1	10 10
(PG)		50	-3	10/10
2,2'-Dipropyl-p,p'-biphenol (PG)	40	25 10	0 +1	10/10 10/10
1,4'-Di-tert-butyl-o,o'-hiphenol	50	40	-6	10/10
(PG)		25	-5	10/10
2,2'-Diallyl-p,p'-biphenol	100	50	-4	10/10
(PG)		25	-2	9/10
p,p'-Isopropylidene-diphenol (PG)	150	100 50	-10 -9	10/10 10/10

4,4'-lsopropylidene-bis(2-tert-butylphenol) (PG)	40	25 10	-5 -6	10/10 10/10
p,p'-Oxydiphenol	150	100	5	10/10
(PG)		50	4	10/10
p-Phenylazopäenol	75	50	-3	10/10
(PG)		25	-3	10/10
3-Methyl-4-pheny lazophenol (PG)	25	10 5	+1 -1	10/10 10/10
Hydroquinone (HOH)	150	100 50	+3	8/10 10/10
2-Quinolinol	150	100	>+18	8/10
(PG)		50	>+22	4/10
3-Quinolinol	50	25	+9	5/10
(PG)		10	+1	9/10
2',5'-Salicyloxylidide, 3-nitro	25	10	+1	10/10
(PG)		5	-1	10/10
2',6'-Salicyloxylidide, 3-nitro	40	25	-2	10/10
(PG)		10	+6	7/10
o-Salicylotoluidide, 3,5'-dinitro	100	100	+5	10/10
(PG)		50	+3	9/10
a-Benzoinoxime	150	100	-5	10/10
(PG)		50	0	10/10
a-Thioglycerol	400	300	0	10/10
(HOH)		100	+1	10/10
Thioglycu c acid - 98%	150	100	-6	10/10
(HOH)		50	-1	10/10
Thiodiglycolic acid 98%	250	200	-6	10/10
(HOH)		100	0	10/10
Thiomalic acid	500	300	-4	10/10
(HOH)		100	+1	10/10
Methylmercaptoacetate (HOH)	400	100 50	+5 -2	10/10 10/10
1,2-Bis-(p-mercaptoethylaminomethyl) cyclobutane (ROH)	250	200 100	>+18 +1	4/10 7/10
6-Methylthio-m-cresol	125	100	>+19	3/10
(PG)		50	+1	9/10
4-Methylthio-m-cresol	150	100	>+19	3/10
(PG)		50	-1	8/10

p-Chlorobenzenethiol	75	50	-4	10/10
(PG)		25	+1	10/10
p-Dimethylaminobenzenethiol	150	100	-3	8/10
(PG)		50	-2	9/10
1-Mercaptoanthraquinone (PG)	750	500 300	>+21 +2	4/10 10/10
1-Hydroxy-4-thiophenylanthraquinone	500	100	-2	10/10
(HOH and PG)		50	+2	10/10
1-Amino-2-thiophenyl-4-hydroxyanthra- quinone (PG and sesame oil)	200 750	500 300	-2 +1	10/10 10/10
Phenylmercaptodiaminoanthrarufin (PG and sesame oil)	150	300	-1	10/10
	300	200	+1	10/10
1-Amino-2-tert-butylphenylmercapto-4- hydroxyanthraquinone (P(f)	250	200 100	+1 +1	10/10 10/10
Thioflavine S	400	300	-2	10/10
(HOH)		100	+1	10/10

ETHERS

	Toxicity	Radiation studies		
Compound and vehicle used for toxicity and radiction tests	Approx. LD ₅₀ (mg./kg.)	Dose (mg./kg.)	Change in SI ₅₀ (days)	Mortality at 30 days
1-Methoxy-2-amino-2-methylpropane	400	300	-7	10/10
(HOH)		100	0	10/10
Bis(2-nitroisobutyl)-2-ethylhexyl phosphate	250	200	-1	10/10
(HOH)		100	+3	10/10
N-(3-Butoxypropyl)taurine, monosodium salt (HOH)	1000	1000 500	+4 +2	7/10 8/9
Cyclobutane-1,2-bis(methylammonium phosphate (HOH)	1000	1000 500	-3 +2	10/10 10/10
Cyclobutane-1,2-bis(methylammonium)	200	100	-4	10/10
dinionochloroacetate		50	-2	10/10
(HOH)		25	+3	9/10
8-Hydroxyethylbenzyl ether	250	200	0	7/10
(PG)		100	+1	10/10
6-Hydroxyethyl ether of orthocresol	250	200	-3	9/10
(PG)		100	+1	9/10
g-Hydroxyethyl ether of butylphenol	100	50	-1	9/10
(PG)		25	-3	10/10
g-Hydroxyethyl ether of m-xylenol	150	100	-5	10/10
(PG)		50	-1	10/10
p-Dimethoxybenzene	400	300	-7	10/10
(PG)		100	+i	8/10
p-Nonylphenyl-β-dimethylaminoethyl ether	150	100	-6	10/10
(PG)		50	-1	9/10
1,6-Bis(p-aminoethylphenoxy)hexane dihydrochloride (HOH)	100	50 25	-4 -3	10/10 7/10
1,6-Bis(p-methylaminomethylphenoxy) hexane dihydrochioride (tIOH)	150	100 50	-2 0	9/10 8/10
Phenylmercurilauryl thioether	500	300	-3	9/10
(PG)		200	0	9/10
2-Methyl-2-nitro-1-propyitosylate (PG)	250	200	+1 +3	10/10 10/10

Bis-[p-(a-diethylaminopropoxy)phenyl] sulfone (HOH)	75	50 25	-1 +1	10/10 10/10
Bis-p-phenyl methane sulfone (PG)	200	100 50	+1 -3	6/10 10/10
μ-Naphthylethyl ether (PG)	100	50 25	-2 0	10/10 10/10
8-Hydroxyethyl ether of β-naphthol (PG)	150	100 50	-5 -1	9/10 7/10
β-Hydroxyethyl ether of orthophenylphenol (PG)	75	50 25	+2 +1	7/10 8/10

KETONES AND PHENONES

	Toxicity	Radiation studies			
Compound and vehicle used for toxicity and radiation tests	Approx. LD ₅₀ (mg./kg.)	Dose (mg./kg.)	Change in ST ₅₀ (days)	Mortality at 30 days	
Methylallyl acetone	1000	500	+1	10/10	
(HOH)		366	-4	10/10	
Acetylacetone	750	500	-2	10/10	
(HOH)		300	-6	10/10	
p-Benzoquinone	7.5	5	-2	10/10	
(HOH)		1	-2	10/10	
2-Methylcyclohexanone	200	100	+1	10/10	
(PG)		50	-5	10/10	
Pulegone	150	100	-1	10/10	
(PG)		50	+2	7/10	
Acetone oxime	250	200	0	10/10	
(PG)		100	+2	10/10	
2-Butanone oxime (PG)	1000	1000 500 250	-4 >+18 +2	10/10 3/10 10/10	
Di(methylcyclopropyl)ketoxime	250	200	-2	10/10	
(HOH)		100	0	9/10	
Cyclohexanone oxime	250	200	-2	10/10	
(PG)		100	0	10/10	
Isonitrosopropiophenone (Lot No. FI-9) (PG)	250	200 100	0 -2	10/10 10/10	
6-Amino-5-hydroxyimino-1,3-dimethyl hydrouracil (PG)	250	200 100	+1 -1	10/10 10/10	
Pyridine-2-aldoxime	200	100	+3	10/10	
(PG)		50	+1	8/10	
Pyridine-3-aldoxime	200	106	+3	10/10	
(HOH)		50	-1	10/10	
Pyridine-4-aldoxime	150	100	+4	10/10	
(PG)		50	+6	9/10	
Isonitrosopropiophenone (Lot No. EL-152) (PG)	200	100 50	+1+8	7/10 8/10	
Pyridine-2-aldoxime o-benzyl ether (PG)	100	50 25	+3 +3	10/10 10/10	

2,3,4a,5,8,8a-Hexahydro-1,4-naphthoquinone (PG)	200	100 50	>+22	4/10 10/10
Methylnaphthoquinone (PG)	15	10 5	+4 +2	7/10 10/10
2-Methyl-1,4-naphthoquinone (Menadione) (PG)	50	40 25	-5 -2	10/10 10/10
7-Chloro-4-(3-octylaminopropyl)amino- quinoline,1-oxide (PG)	40	25 10	-2 +2	10/10 10/10
Sodium β-naphthoquinone-4-sulfonate (HOH)	625	300 200	-4 0	10/10 10/10
2-Oxo-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11- β-hexahydro-2H-benzoquinolizine (PG)	250	200 100	+3 +5	10/10 10/10
N-1-Anthraquinonyl-2,3-dichloropropion- amide (PG)	200	100 50	-2 +1	10/10 10/10
1-Thiophenylanthraquinone (Sesame oil)	500	500 300	-1 +2	10/10 10/10
2-Thiophenylanthraquinone (PG)	150	100 50	-3 +3	10/10 10/10
1-Amino-2-thiophenylanthraquinone (PG)	> 1000	500 300	+2 +4	10/10 10/10
1-Amino-4-thiophenylanthraquinone (PG)	> 1000	500 300	0 +3	10/10 10/10
Dimethylsulfoxide (DMSO) (100%)	7500	5000 2500	>+22 +4	1/10 8/10
Tetramethyldiaminothiobenzophenone (PG)	250	200 100	+3 -1	13/10 10/10
2-Nitro-4-acetyl-2'-aminodiphenyl sulfide (PG)	150	100 50	+4 -5	10/10 10/10
1-Amino-2-benzylmercapto-4-hydroxy- anthraquinone (PG)	150	100 50	-1 +4	10/10 10/10

ACIDS AND THIOACIDS

	Toxicity	Radiation studies		
Compound and vehicle used for toxicity and radiation tests	Approx. LD ₅₀ (mg./kg.)	Dose (mg./kg.)	Change in ST ₅₀ (days)	Mortality at 30 days
Cacodylic acid (HOH)	750	500 200	-3 +4	10/10 6/10
Cyanoacetic acid (HOH)	200	100 50	-5 -3	10/10 10/10
Ethylenediaminetetraacetic acid (EDTA) (PG)	250	200 100	-1 +2	10/10 10/10
Bis(diaminoethyl ether)-N,N,N'-N'- tetraacetic acid (PG)	250	200 100	-4 +1	10/10 9/10
Ethyleneglycol-bis-(aminoethyl ether) tetraacetic acid (PG)	150	300 200	-10 -1	10/10 10/10
Levulinic acid (HOH)	450	300 100	-10 >+22	10/10 4/9
Chrysanthemummonocarboxylic acid (PG)	150	100 50	-5 -1	10/10 10/10
3-Methylenecyclobutanecarboxylic acid (HOH + NaHCO ₃)	750	500 300 100	-4 0 -1	10/10 10/10 10/10
2-Aminocyclobutanecarboxylic acid hydrochloride (HOH)	>1000	1000 500 200	-4 -3 0	10/10 10/10 10/10
trans-1,2-Cyclobutanedicarboxylic acid (HOH)	400	300 200	0 -1	9/10 10/10
3-Methyl-2-cyclobutene-1,2-dicarboxylic acid (HOH)	200	100 50	0	9/10 10/10
1,2-Diaminocyclohexanetetraacetic acid (PG)	150	100 50	-3 -2	10/10 9/10
Trisodium-2-(hydroxycyclohexyl)ethylenedi- amine triacetate (PG)	400	300 200	-4 +3	10/10 9/10
a-Imino-p-methoxybenzylmercaptoacetic acid (PG)	250	200 100	-7 0	9/10 10/10

Indole-3-acetic acid (PG)	150	16° 60	+1 +3	10/10 10/10
N-(2,3-Xylyl)anthranilic acid: mefenamic acid (PG)	200	100 50	+1 -2	10/10 10/10
N-(3,5-Dichloro-p-tolyl)anthranilic acid (HOH + NaHCO ₃)	100	50 25	0 -1	7/10 8/10
N-(a,a,a-Trifiuoro-m-tolyl)anthranilic acid; flufenamic acid (PG)	150	50 25	+3 +1	10/10 10/10
N-(3-Sulfamoyl-2,6-xylyl)anthranilic acid (HOH + NaHCO ₃)	400	300 200	+3 +2	7/8 10/10
Ethylenediamine-di(o-hydroxyphenyl)acetic acid (PG)	350	100 50	1 1	10/10 10/10
N-(8-Amino-1-anthraquinonyl)anthranilic acid (HOH + NaHCO ₃)	750	500 300	-5 -8	9/10 8/10
3-(2-Aminoethylthio)propionic acid (HOH)	>1000	500 300	-5 -5	10/10 10/10
meso-2,3-Dimercaptosuccinic acid (HOH)	500	300 200	-7 -1	10/10 10/10
5,8,11,14-Eicosatetranoic acid (PG)	75	50 25	-5 -1	10/10 10/10
2-Brom-v-lysergic acid diethylamide (HOH)	75	25 10	-2 0	10/10 10/10
2-Aminoethanethiosulfuric acid (HOH)	400	300 100	+3 +3	7/10 9/10
3-Chloro-1-propanesulionic acid, monosodium salt (HOH)	750	500 200	+6 +2	6/10 9/10
2-Carboxyphenylthioglycolic acid (HOH)	250	200 100	-8 -3	9/10 9/10
4-Chloro-2-methylphenylthioglycolic acid (PG)	150	100 50	-11 -2	10/10 10/10
Alanine: 2-methyl- (HOH)	750	500 300	-1 -1	10/10 10/10
DL-β-(3,4-Dihydroxyphenyl)alanine (HOH)	500	300 200	-1 0	10/10 10/10

L-Cysteine hydrochloride (HOH)	1250	1000 500	-6 -5	10/10 10/10
N-Acetyl-n-cysteine (HOH)	400	300 200	-4 0	10/10 10/10
(Carboxymethyl)trimethylammonium-N- acetyl-L-cysteinate (HOH)	>1000	1000 500	0	10/10 10/10
Glutathione (HOH)		1000	+1	10:10
Glutathio e ascorbate, 63.57%-36.43% (HOH)	>100	100 50	+2 +1	9/10 9/10
Glutathione ascorbate, 1:10 (HOH)	>100	100 50	+2 -1	10/10 10/10
Glutathione ascorbate with calcium phytate (CaMg inositol hexaphosphate) (HOH)	>100	100 50	+2 -2	10/10 10/10
Glutathione (glutamyl-cysteinyl-glycine, in molecular relation) (HOH)	>100	100 50	+2	9/10 10/10
N-Acetyl-DL-penicillamine (PG)	400	300 200	-4 +1	10/10 10/10

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ESTERS

	Toxicity	Radiation studies		
Compound and vehicle used for toxicity and radiation tests	Approx. LD ₅₀ (mg./kg.)	Dose (mg./kg.)	Change in ST ₅₀ (days)	Mortality at 30 days
Methyl chloroformate (HOH)	40	25 10	0 -5	10/10 10/10
Acetic acid: 2-methoxy-1-methyl ethyl ester (HOH)	750	500 200	+1 -5	10/10 10/10
3-(Amidinothio)propionic acid, ethyl ester, monohydrochloride (HOH)	250	200 100	+2 -2	10/10 10/10
Nitriloacetic acid trisodium salt monohydrate (HOH)	500	300 100	-3 +2	10/10 10/10
Dipotassium methanearsonate (HOH)	750	50% 230	-4 +1	10/10 10/10
Monoammonium methanearsonate (HOH)	>1000	1000 500	-3 -3	10/10 10/10
Sodium cacodylaie (HOH)	>1000	1000 500	-5 -4	10/10 10/10
Calcium methanearsonate (HOH)	500	300 100	-3 +1	10/10 10/10
Magnesium cacodylate (HOH)	750	500 200	-4 -3	10/10 10/10
Magnesium methanearsonate (HOH)	>1000	1000 500	0 -1	10/10 10/10
Dimercurous methanearsonate (HOH)	75	50 10	-11 -7	10/10 10/10
Disodium methanearsonate (HOH)	>1000	1000 500	5 2	10/20 S/10
Copper methanearsonate (HOH + NaHCO ₃)	15	10 5	-6 +2	10/10 9/10
Dibutyl fumarate (PG)	250	200 100	+1 +2	10/10 10/10
Di-2-ethylhexyl fumarate (PG)	250	200 100	+1 +1	10/10 10/10
Dibutyl maleate (PG)	150	100 50	-1 +2	10/10 10/10

Di-2-ethylhexyl maleate (PG)	>1000	1000 500	+1	10/10 10/10
Ethyl-1-methyl propyl diethyl malonate (PG)	200	100 50	+1 -2	10/10 10 10
Dimethyl-1,2-cyclobutanedicarboxylate (HOH)	>1000	1500 1000 500	+2 -2 0	9/10 8 10 10/10
cis-1,2-Diisopropylcyclobutanedicarboxylate (PG)	750	500 300 100	-4 -4 +5	10 10 10/10 5/10
trans-1,2-Diisopropylcyclobutanedicarboxyl- ate (PG)	250	200 100	-3 +2	10, 10 10/10
Diisodecyl-1,2-cyclobutanedicarboxylate (PG)	750	500 300	0	10/10 9 10
Hexamethylenediammonium cyclobutane-1,2- dicarboxylate (HOH)	>1000	100C 500	0 +2	10·10 10/10
Cyclobutane-1,2-bis(methylammonium) adirate (HOH)	>1000	1000 500	-3 -1	10 10 10, 10
Bis-(2,4,5-trichlorophenyl)-1,2-cyclobutane dicarboxylate (PG)	250	200 100	0 +2	10 10 10/10
Methyl-p-nitrobenzoate (PG)	200	100 50	0 -2	9/10 10/10
Ethyl-p-nitrobenzoate (PG)	250	200 100	0 +2	10 10 10,10
Ethyl-N-(p-nitrobenzenesulfonyl)urethane (PG)	200	100 50	-3 +16	9·10 5/10
Ethyl-N-o-toluenesulfonylurethane (PG)	250	200 100	+6 +1	8/10 10/10

AMIDES AND THIOAMIDES

	Toxicity	Radiation studies			
Compound and vehicle used for toxicity and radiation tests	Approx. LD ₅₀ (mg./kg.)	Dose (mg./kg.)	Change in ST ₅₀ (days)	Mortality at	
N,N-Dimethylacetamide	>1000	1000	+1	10/10	
(HOH)		500	0	10/10	
Acetamide: 2-(2-hydroxyethoxy)- (PG)	100	50 25	+2 -6	10/10 10/10	
n-Cyanoacetamide	>1000	1000	-3	10/10	
(HOII)		500	0	10/10	
a-Methylmercapto-a,a diethylacetamide (PG)	750	500 200	-5 +2	10/10 10/10	
a-Ethylmercaptoisobutyramide	>1000	1000	+5	6/10	
(PG)		500	-3	10/10	
a-Allylmercaptoisobutyramide	250	200	0	10/10	
(PG)		100	+1	10/10	
a-A!lylmercapto-a,a-diethylacetamide	400	250	-2	10/10	
(PG)		100	0	10/10	
a-I.:opropylmercaptoisobutyramide	750	500	-1	10/10	
(PG)		200	+3	10/10	
N-Acryloyltaurine, monosodium salt	>1000	1000	0	10/10	
(HOH)		500	+2	10/10	
N-Methyl-a-crotylmercaptoisobutyramide (PG)	750	500 300	- 7 -1	10/10 16/10	
a-Propargylmercapto-a,α-diethylacetamide	250	200	-1	9/10	
(PG)		100	-3	10/10	
a-Butylmercaptoisobutyranıde	250	200	-1	10/10	
(PG)		100	-1	10/10	
2,2'-Thio-bis-acetamide	625	500	+ 2	10/10	
(PG)		300	+ 3	10/10	
trans-1,2-Cyclobutanedicarboxamide	>1000	1000	+1	10/10	
(HOH)		500	+1	10/10	
N,N'-di-tert-Butylcyclobutane-1,2-dicarbox- amide (PG)	250	200	-2 +2	10/10 10/10	
N,N'-Bis(1,1,3,3-tetramethylbutyl)-1,2- cyclobutanedicarboxamide (PG)	250	200 100	0 -4	10/10 10/10	

N,N'-(a-Naphthyl)-1,2-cyclobutanedicarbox-	275	250	6	10/10
amide		200	+2	6/10
(PG)		100	- 4	10/10
N,N'-(β-Naphthyl)-1,2-cyclobutanedicar-	>1000	500	+2	6/10
boxamide		300	-5	10/13
(PG)				}
o-Hydroxy-N,N-diethylbenzamide	200	100	-2	10/10
(PG)		50	-3	10/10
p-Toluenesulfanamide	250	200	-2	10/10
(PG)		100	+3	10/10
Carbutamide	250	200	-1	10/10
(PG)		100	+3	8/10
4',3-Dinitrosalicylanilide	25	10	-2	10/10
(PG)		5	+3	10/10
4'-Chloro-3-nitrosalicylanilide	15	10	0	9/10
(PG)		5	+2	10/10
4'-Chloro-5-nitrosalicylanilide	40	25	0	10/10
(PG)		10	+4	9/10
C'-Chloro-3-nitrosalicylanilide	8	5	+3	8/10
(PG)		1	0	10/10
3'-Chloro-5-nitrosalicylanilide	15	10	+1	9/10
(PG)	ļ	5	+3	10/10
4'-Fluoro-3-nitrosalicylanilide	15	10	_7	10/10
(PG)		',	+6	10/10
4'-Bromo-3-nitrosalicylanilide	15	10	0	10/10
(PG)		5	+5	10/10
3'-Iodo-3-nitrosalicylanilide	15	. 0	+3	10/10
(PG)		5	0	10/10
4'-Iodo-3-nitrosalicylanilide	15	10	-3	10/10
(PG)		5	+4	10/10
3',4'-Dichloro-3-nitrosalicylanilide	15	10	+3	10/10
(PG)		5	+8	8/10
2'-Chloro-5'-trifluoromethyl-3-nitrosalicylani-	8	5	0	10/10
lide (PG)		1	+2	10/10
N-p-Toluenesulfonyl, isoquinuclidylform-	150	100	-4	8/10
amide	1	50		10/10
(PG)	i	1	1	1

N,N-Bis(2-cyanoethyl)-N-4-hydroxy-1- anthraquinonylsulfonilamide (PG)	400	300 100	+2 -3	8/10 10/10
Bis-(2-amino-4-sulfonam.dophenyl) disulfide (PG)	150	100 50	-4 -1	10/10 10/10
N,N'-Bis(2-methoxyethyl)dithiooxamide (PG)	400	250 100	0	10/10 9/10
N,N'-Di-tert-butyldithiooxamide	40	25	-2	10/10
(PG)		10	+2	10/10
N,N'-Dioctadecyldithiooxamide	150	100	0	10/10
(PG)		50	+7	6/10
Bis-didodecyldithiooxamide	250	200	-4	10/10
(PG)		100	0	10/10
Thiopyrazinamide	150	100	0	10/10
(PG)		50	-2	10/10
p-Aminothiobenzamide	75	50	0	10/10
(PG)		25	-3	10/10
N,N-Dimethyl-a,a-diphenylthioacetamide	250	200	-5	10/10
(PG)		100	-1	10/10
N,N'-Methylene-bis-(thioisonicotinamide; hydrate (PG)	250	200 100	-6 -1	10/10 10/10

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CARBAMATES AND THIOCARBAMATES

	Toxicity	Radiation studies			
Compound and vehicle used for toxicity and radiation tests	Approx. LD ₅₀ (mg./kg.)	Dose (mg./kg.)	Change in ST ₅₀ (days)	Mortality at 30 days	
Dinvethylcarbamyl chloride	>1000	1000	-2	10/10	
(HOH)		500	+2	10/10	
Diethylcarbamyl chloride	750	500	-1	10/10	
(HOH)		300	+1	10/10	
Ethyl-N,N-di-N-butylcarbamate	150	100	-8	10/10	
(PG)		50	-7	10/10	
Ethyl-N,N-butylcarbamate (PG)	250	200 100	-4 0	10/10 8/16	
Carbamic acid: 2-aminoethyl ester (HOH)	>1000	1000 500	+3 -1	10/19 10/10	
N,N'-Dicarbamylformamidine (PG)	250	200 100	+1 -2	8/10 10/10	
2-Nitro-2-methyl-1,3-propanedioldicarbamate	>1000	1000	-3	10/10	
(HOH)		500	-3	10/10	
1,2-C ₃ · obutanedimethylcarbamate (PG)	>1000	1000 500	0 +3	9/10 10/10	
1-Methylammonium-2-carbamylmethyl cyclobutane (HOH)	750	500 300	-3 +2	9/10 10/10	
γ-Phenylpropylcarbamate	150	100	-4	10/10	
(PG)		50	0	10/10	
Isopropyl-N-phenylethylcarbamate	150	100	-4	10/10	
(PG)		50	-4	10/10	
Ethyl-N-(m-nitrophenylsulfonyl)carbamate	100	50	-10	10/10	
(PG)		25	-4	10/10	
Ethyl-N-(p-chlorophenyl)carbamate	150	100	-6	10/10	
(PG)		25	0	6/10	
2-Nitroisobutyl-N-phenylcarbamate	750	500	-2	10/10	
(PG)		200	-5	10/10	
2-Nitro-2-methyl-1,3-propanediol-bis(N- phenylcarbamate) (PG)	150	100 50	2 3	9/10 10/10	

n-Amyl-N-butylsulfonylcarbamate (sodium salt) (HOH)	750	500 200	-5 -1	10/10 10/10
Ethyl-N-(n-octylsulfonyl)carbamate (PG)	150	100 50	+-6 2	7/10 10/10
1-Methylammonium-2-dithiocarbamyl methylcyclobutane (HOH)	1000	300 100	+1	10/10 10/10
Thiocarbamic acid, p-hydroxyphenyl ester (PG)	150	100 50	+3 -1	7/10 10/10

UREAS AND THIOUREAS

	Toxicity	Radistion studies			
Compound 5:1d vehicle used for toxicity and radiation tests	Approx. LD ₅₀ (mg./kg.)	Dose (mg./kg.)	Change in ST ₅₀ (days)	Mortality at 30 days	
Acetylurea (HOH)	>1000	1000 500	0	10/10 10/10	
2-Ailyl-2-thiopseudourea, monohydrobromide (HOH)	250	200 100	1 +2	10/10 10/10	
2-Methyl-2-thiopseudourea, monohydro- bromide (HOH)	750	500 300	>+17 >+19	3/10 2/10	
2-Methyl-2-thiopseudourea sulfate (HOH)	400	300 300 100	>+22 >+22 +7	3/10 1/9 6/10	
2,2'-Trimethylene-bis(2-thiopseudourea), dihydrobromide (HOH)	250	200 100	0 +1	6/10 10/10	
Tetramethylthiuram monosulfide (PG)	150	100 50	+2 >+15	10/10 3/10	
β-Diisobutylaminoethylisothiourea dihydrochloride (HOH)	75	50 25	0 -2	10/10 10/10	
2,2'-Pentamethylene-bis(1-acetyl·2- thiopseudourea), dihydrochloride (HOH)	250	200 100	-1 -3	10/10 10/10	
2-Decyl-2-thiopseudoures, monohydrochloride (HOH)	75	25 10	0 +4	9/10 6/10	
2-(Cyanomethy:)-2-thiopseudourea, mono- hydrochloride (HOH)	750	500 300	+7 0	5/10 8/10	
2-(Amidinothio)butyric acid, monohydro- bromide (HOH)	750	500 300	-10 -2	10/10 9/10	
4-(Amidinothio)butyric acid, monohydro- bromide (HOH)	100	50 25	-8 0	10/10 10/10	
2-(2-Hydroxyethyl)-2-thiopseudourea, monohydrobromine (HOH)	400	300 200	-3 +1	10/10 7/10	

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1-o-Tolyl-2-thiourea	150	100	+3	8/10
(PG)		50	-2	10/10
2-(2-Phenoxyethyl)-2-thiopseudourca, monohydrochloride (HOH)	40	25 10	-2 +1	10/10 10/10
p-Acetylaminoacetophenone thiosemicarba- zone (PG)	50	25 10	-2 -1	10/10 7/10
2-(p-Nitrobenzyl)-2-thiopseudourea, monohydrochloride (HOH)	75	50 25	+1 -4	10/10 10/10
p-Nitrobenzylisothiourea hydrobromide	150	100	-2	9/10
(HOH)		50	-4	10/10
p-Nitrophenylsulfonylurea	750	500	+2	8/10
(PG)		300	-2	10/10
N-Sulfanilylurea	>1000	1000	+1	10/10
(HOH)		500	-1	9/10
N-(p-Acetylaminobenzenesulfonyl)ethyl- urethane (PG)	750	500 300	-3 -2	10/10 10/10
p,p'-Biphe ıylene-bis-1,1'-(2-thiourea) (PG)	75	50 25	6 6	10/10 10/10
Di-p-methoxyphenylthiourea	750	500	-4	10/10
(PG)		300	-4	10/10
Di-p-chlorophenylthiourea	150	100	0	10/10
(PG)		50	-3	10/10
1-Isothiourea-2-dibenzylaminoethane dihydrochloride (HOH)	100	50 25	-6 -1	10/10 9/10
1-(p-Phenylazo)phenyl-2-thiourea	150	100	+1	7/10
(PG)		50	-2	9/10
Bis-[p,p-(isothioureidomethyl)phenyl] sulfone dihydrochloride (HOH)	75	50 25	~5 ~5	10/10 10/10

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AMINES

	Toxicity	Radiation studies			
Compound and vehicle used for toxicity and radiation tests	Approx. LD ₅₀ (mg./kg.)	Dose (mg./kg.)	Change in ST ₅₀ (days)	Mortality at 30 days	
Methylamine hydrochloride (HOH)	>1000	1000 500	-2 -2	10/10 10/10	
N-(2-Nitro-2-methylbutyl)dimethylamine (PG)	200	100 50	+1 +3	10/10 10/10	
N-(2-Nitroisobutyl)-N-methylglucamine (HOH)	>1000	1000 500	-2 0	10/10 10/10	
Benzyloctylmethylamine (PG)	100	50 25	+3 -1	10/10 8/10	
Ethylamine: 2-bromohydrobromide (HOH)	>1000	200 100	-2 +2	10/10 10/10	
Ethylamine: 2-methoxy (65%-70% in HOH) (HOH)	400	200 100	-1 -4	10/10 10/10	
2-Bromoethylamine hydrobromide (HOH)	400	200 100	-6 0	10/10 10/10	
2,2'-Dithio-bis-(ethylamine) dihydrochloride (HOH)	750	300 200	>+16	0/10 7/10	
Di(β -p-methoxyphenylethyl)amine hydrochloride (PG)	500	300 200	+3 -1	8/10 10/10	
3-(N-Methylisopropylamino)-3-methyl-2- butanone hydrochloride (HOH)	150	100 50	-1 0	10/10 10/10	
tert-Butyl-tert-amylamine hydrochloride (HOH)	100	50 25	-4 -2	10/10 10/10	
3-tert-Butylamino-3-methyl-1-butene hydrochloride (HOH)	75	50 25	0 5	10/10 10/10	
3-tert-Butylamino-3-methyl-1-butyne hydrochloride (HOH)	75	50 25	-4 -2	10/10 10/10	
3-Methyl-N-(2-o-propylphenoxyethyl) butylemine, monohydrochloride (HOH)	>1000	1000 500	-10 -3	9/10 10/10	
3,5-Dimethyl-3-amino-1-hexyne hydrochloride (HOH)	400	100 50	-5	10/10 10/10	

N-(2-Nitroisobutyl)-2-ethylhexylamine (PG)	250	200 100	-2 +3	10/10 10/10
p-Isopropylbenzylhenylamine sulfate (PG)	150	100 50	-10 +1	10 ′10 10 10
N-Heptyltaurine, monosodium salt (HOH)	>1000	1000 500	+9	5 10 10 10
p-Isopropylbenzylheptylamine sulfate (PG)	75	50 25	_7 _4	10/10 16/10
Octylamine (PG)	100	50 25	-1 +6	10/10 9 10
Benzyloctylamine (PG)	100	70 25	-7 +1	10 10 9 10
p-Isopropylbenzyloctylamine (PG)	75	25 10	-8 +1	10/10 9 10
Dodecylamine (PG)	50	25 10	-3	10/10 10/10
N-Dodecyltaurine, monosodium salt (HOH)	400	300 200	0 +2	10/10 10 10
Hexadecylamine (PG)	200	100 50	1 +1	10, 10 10, 10
Octadecylamine (PG)	250	200 100	-3	10/10 10/10
N',N'-Dimethyl-1,2-butanediamine (PG)	150	100 50	-4 +1	10/10 10 '
N,N'-Bis(β-mercaptoethyl)hexamethylene diamine (PG)	350	200 100	5 0	10/10 8/10
Armeen-CD-oleylamine (PG)	25	10 5	+2 +3	10,10 10 10
Armeen-TD-hydrogenated tallow amine (PG)	200	100 50	-1 +3	10/16 10 10
trans-1,2-Bis(aminoethyl)cyclobutane (HOH)	50	40 25	0 -3	9/10 10/10
1,3-Diamino-2,2,4,4-tetramethylcyclobutane (HOH)	450	200 100	-1 +1	10/10 10/10
Cyclobutane-1,2-bis(methylammonium) distearate (PG)	>1000	1000 750 500 500	-1 >+19 0 +2	5/10 3/10 5/10 9/10

Tetramethylammonium chloride	25	7.5	+2	9/10
(HOH)		5.0	+2	10/10
Fetramethylammonium iodide	40	10	0	10/10
(HOH)		5	+2	10/10
Aniline hydrochloride	750	500	-4	10/10
(HOH)		200	-2	10/10
o-Toluidine	150	100	-1	10/10
(PG)		50	-2	10/10
n-Toluidine	150	100	-1	10/10
(PG)		50	-1	10/10
o-Toluidine	50	25	-2	10/10
(PG)		10	+1	10/10
N-Acetyl-m-methylthioaniline	750	500	-2	10/10
(PG)		300	-5	10/10
p-Nitroaniline	250	200	-3	10/10
(PG)		100	+5	10/10
o-Phenylenediamine dihydrochloride	250	200	-3	10/10
(HOH)		100	-1	10/10
m-Phenylenediamine dihydrochloride	150	100	-4	9/10
(HOH)		50	0	10/10
2-Chlorobenzylethylenediamine (PG)	150	100 50	-2 -4	10/10 9/10
N,N-Dimethyl-p-phenylenediamine dihydrochloride (HOH)	40	25 10	+2	10/10 10/10
Diphenylbenzidine	>1000	500	-2	10/10
(sesame oil)		300	+1	10/10
o,o-Dithio-bi s-aniline	75	50	-6	8/10
(PG)		25	-1	9/10
Benzyl-2,4-dichlorobenzylamine hydrochloride (PG)	250	200 100	-5 +2	10/10 6/10
Benzyl-3,4-dichlorobenzylamine hydrochloride (PG)	150	100 50	-3 -1	10/10 10/10
N-(2-Dimethylaminoethoxy)-N-(3,4,5- trimethoxybenzoyl)benzylamine hydro- chloride (Tigan) (HOH)	400	300	+2	7/10 9/10
Dimethyl-a-naphthylamine	75	50	-3	10/10
(PG)		25	0	10/10

N-(1-Naphthyi)ethylenediamine dihydro- chloride (HOH)	150	100 50	+1 -2	10/10 10/10
2-Nitro-4-acetyl-2'-formylaminodiphenyl sulfide (PG)	250	200 100	-2 -7	10/10 10/10
N-(γ-Dimethylaminopropyl)-2-methyl thiodiphenylamine hydrochloride (HOH)	50	25 10	+2	10/10 10/10
Hydroxylamine hydrochloride (HOH)	100	50 25	-4 -1	10/10 10/10
o-Benzylhydroxylamine hydrochloride (HOH)	250	200 100	-2 +1	10/10 9/10

GUANIDINES AND NITRILES

	Toxicity		Radiation studies			
Compound and vehicle used for toxicity and radiation tests	Approx LD ₅₀ (mg./kg.)	Dose (mg./kg.)	Change in ST ₅₀ (days)	Mortality at 30 days		
Cyanoguanidine (HOH)	> 1000	1000 500	0	10/10 10/10		
β-Phenethylbiguanide hydrochloride (HOH)	150	100 50 25	+2 -1 +1	4'4 10:10 10/10		
Dipyridylguanidine trihydrochloride (HOH)	750	500 300	$\begin{array}{c c} -2 \\ -7 \end{array}$	10/10 10/10		
Methyl cyanoacetate (HOH)	750	500 300	+5 2	10/10 13/10		
Dimethylcyanamide (HOH)	40	25 10	-4 -2	10/10 19/10		
Propionitrile (HOH)	50	25 10	-4 +1	9/10 10/10		
Acrylonitrile (HOH)	?5	75 50 25	+1 +18 -5	10/10 2/10 19/10		
Cyanoacetamide (HOH)	750	500 300	0 -4	10/10 10/10		
Adiponitrile (HOH)	40	25 10	+1 -4	10/10 10/10		
Ethyl cyanoacetate (HOH)	750	500 300	+2 -4	10/10 10/10		
Methacrylonitrile (PG)	100	50 75	+3 >+19	5/10 1/10		
Hydroxyacrylonitrile (HOH)	>1000	1000 500	-2 0	10/10 10/10		
a,a'-Azodiisobutyronitrile (PG)	25	10 5	-2 -3	10/10 10/10		
trans-1,2-Dicyanocyclobutane (HOH)	275	250 100 50 50 25	7 2 +10 0 +1	10/10 10/10 6/10 10/10 10/10		
1,2-Dicyanocyclobutene-1	150	100 50	0 +1	9/10 10/10		

3-Methylenecyclobutane carbonitrile (HOH)	250	200 100	0	10/10 10/10
Chlorinated-1,2-dicyanocyclobutane (Lot No. ST-15) (PG)	75	50 25	-4 -1	9/10 9/10
trans-2-Cyanocyclobutanecarboxamide (PG)	250	250 200 200 150 150 100 50	+3 +1 0 +15 +6 +3 +4	10/10 5/10 7/10 5/10 10/10 6/10 10/10
2,2-Dimethyl-3-methylenecyclobutane carbonitrile (HOH)	200	100 50	+2	10/10 10/10
Chlorinated-1,2-dicyanocyclobutane (Lot No. ST-24) (PG)	400	209 100 50	-4 -3 -4	10/10 10/10 10/10
Tetra-\$\beta\$-cyanoethyl-1,2-bis(aminomethyl) cyclobutane (HOH)	400	100 50	0	10/10 9/10
o-Chlorobenzonitrile (PG)	150	100 50	-4 +3	10/10 7/10
p-Chlorobenzonitrile (PG)	150	100 50	-2 0	10/10 10/10
Phenylacetonitrile (PG)	40	10 5	-6 -4	10/10 10/10
a-Dimethylaminophenylacetonitrile (PG)	40	25 10	+3 -1	8/10 9/10
4-Hydroxybenzonitrile (HOH)	200	100 50	-6 -5	10/10 10/10
m-Trifluoromethylphenylacetonitrile (PG)	100	50 25	+1 +3	8/10 7/10
3,4-Dihydro-2-cyano-2H-pyran (HOH)	250	200 100	-1 +2	10/10 10/10
Thiocyanic acid, a-3,a-5-bis(dimethylamino)- 4-hydroxy-3,5-xylyl ester (PG)	75	50 25	+5 +2	7/10 9/10
Diphenylacetonitrile (PG)	200	100 50	-3 +2	10/10 10/10
4,4'-Biphenyldicarbonitrile (PG)	75	50 25	-5 -7	9/10 10/10

β-Cyanoethylmercaptan	100	75	+1	10/10
(HOH)		50	+3	10/10
Sodium s-sulfopropionitrile (HOH)	>1000	500 300	-1 -2	10/10 10/10
p-Cetoxyphenylisothiocyanate	150	100	-5	10/10
(PG)		50	+1	10/10
Cyclohexylcyanoethylethanolamine	200	100	-4	10/10
(PG)		25	-1	10/10
p-(n)Dodecoxyphenylisot .iocyanate	150	50	-2	10/10
(PG)		25	-1	10/10
2-Thio-m-thiazone-2,4-dione	750	400	-1	10/10
(HOH)		200	-4	10/10

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HYDRAZINES

	Toxicity	Radiation studies			
Compound and vehicle used for toxicity and radiation tests	Approx. LD ₅₀ (mg./kg.)	Dose (mg./kg.)	Change in ST ₅₀ (days)	Mortality at 30 days	
Hydrazine sulfate (HOH)	250	100 50	-2 -2	10/10 10/10	
(3-Octylaminopropyl)hydrazine (PG)	15	10 5 1	+3 +2 -5	10/10 10/10 10/1	
29 (2,2-Dimethylhydrazino)-3,6,9,12,15,18, 21,24,27-nonathianonacosane-1-thiol (PG)	400	400 300 250 200 50	-3 >+17 -4 -6 -4	10/10 4/10 10/10 10/10 8/10	
Methylcyclopropanecarbonylhydrazine (HOH)	40	25 19	0 -3	10/10 10/10	
1,2-Cyclobutanedicarboxylic acid dihydrazide (HOH)	>1000	500 300	-1 0	10/10 10/10	
1,2-Cyclobutanedicarboxylic acid mono(2',2'-dimethyl)hydrazide (HOH)	> 1000	1000 500	-1 +4	10/10 10/10	
Acetphenylhydrazine (PG)	150	100 50	-1 -1	10/10 10/10	
N-Benzyl-N'-isopropylhydrazine hydro- chloride (HOH)	250	200 100 20	-2 0 -4	10/10 10/10 10/10	
3,4,5-Trimethylacetophenonethiosemicarba- zone (PG)	75	50 25	10 8	10/10 10/10	
3,3'-Thiodipropionic acid, bis(D-galactosyl- methylenehydrazide) (PG)	750	500 300	0 -1	10/10 19/10	
1-Isonicotinyl-2-dimethylhydrazine (PG)	400	300 100 30	+1 +1 -2	10/10 10/10 9,10	
1-Ethyl-2-isonicotinylhydrazine (HOH)	150	100 50 10	+1 0 -5	10/10 10/10 10/10	
1-Isonicotinyl-2-ethyliden^hydrazine (PG)	150	100 50 10	+1 0 -2	10/10 10/10 7/10	

$[\alpha-(Methylmercapto)-4-pyridylmethylene] hydrazine (PG)$	200	100 50 10	-2 -2 -4	10/10 10/10 6/10
a-(Benzylmercapto)-4-pyridylmethylene hydrazine (PG)	3	1.0 0.5 0.1	+1 +2 -5	10/10 10/10 10/10
1-Isonicotinyi-2-glucosylhydrazine (PG)	400	300 100 30	-2 0 -4	10/10 10/10 10/10
N,N'-Ethyleneidene-bis(isonicotinyl- hydrazine) (Safflower oil)	>1000	1000 500	0 -3	10/10 13/10

THIOPHENES, OXACYCLOPENTANES, AZACYCLOPENTANES, AND AZACYCLOHEXANES

	Toxicity	Radiation studies			
Compound and vehicle used for toxicity and radiation tests	Approx. LD ₅₀ (mg./kg.)	Dose (mg./kg.)	Change in ST ₅₀ (days)	Mortality at 30 days	
2-Acetothiophene (PG)	40	10 200	-2 -1	10/10 10/10	
4'-Hydroxy-5-nitro-2-furanacrylanilide (PG)	400	300 200	+1 -1	7/10 10/10	
4'-(2-Chloroethylthio)-5-nitro-2-furan- acrylanilide (PG)	260	100 50	-3 -1	10/10 10/10	
p-{3-(5-Nitro-2-furyl)acrylamido]benzyl- thioacetic acid, methyl ester (PG)	750	500 300	-3 -1	5/10 10/10	
N-Butylenepyrrolidine (HOH)	50	25 10	-2 +3	10/10 9/10	
Monothiosuccinimide (PG)	150	100 50	+3 +10	6/10 6/10	
N-Methylmonothiosuccinimide (PG)	250	200 100	-2 +3	7/10 10/10	
2-[2-(1-Fyrrolid [:] nyl)ethyl]-2-thiopseudourea, dihydrochloride (HOH)	150	100 50	-2 -1	10/10 10/10	
N-Phenylmonothiosucci, mide (PG)	250	200 100	+22 +1	4/10 10/10	
N-(p-Methoxyphenyl)monothiosuccinimide (PG)	250	200 100	-1 +4	5/10 6/10	
Pyrrolidinopropiophenone hydrochloride (HOH)	75	50 25	-3 -2	10/10 10/10	
1-(1-Pyrrolidinocyclohexyl)methylthio- sulfuric acid, zwitterion (I) (HOH)	150	100 50	+2 0	5/6 10/10	
1,2-Cyclobutanedicarboxamide (HOH)	> 1000	1500 1000 1000 500	0 +4 -1 +1	10/10 5/10 10/10 6/10	
1-Aza-2-imino-7-oxacycloheptane (HOH)	> 1000	1500 1000 1000 500	+2 +5 -1 -2	10/10 6/10 10/19 10/10	

1-Aza-2,7-diiminocycloheptane (HOH)	250	200 100	0 +2	10/10 10/10
N-(a-Naphthyl)-1,2-cyclobutanedi-	750	500	-4	10/10
carboximide		300	-3	10/10
(PG)		100	+2	8/10
N-(β-Naphthyl)-1,2-cyclobutane dicarboximide (PG)	400	300 100	+2 +3	10/10 10/10
5-Acetyl-3-(2-2minoethyl) indole hydrochloride	200	100	>+19	1/9
(HOH)		25	>+19	4/10
3-(2-Aminopropyl)-5-indolyl maleate salt (HOH)	625	500 300	+4 -1	3/8 6/10
DL-3-(2-Amino-1-methylethyl)-5- propionylindole hydrochloride (HOH)	200	100 50	+1+2	13/17 8/10
pl3-(Aminopropylene)indolyl-5-phenyl- ketone hydrochloride (HOH)	100	50 25	+3 -2	8/10 9/9
3-Amino-9-ethylcarbazole (FG)	150	100	-10 +1	10/10 5/10
3,6-Diamino-9-ethylcarbazole (PG)	150	100 50	-2 0	10/10 9/10
3-Methyl-5-carboxytetrahydro-4-carboline (PG)	150	100 50	0 +1	10/10 10/10
Ajmaline	75	50	+2	9/10
(PG)		25	+1	10/10
Aspidospermine	40	25	-1	10/10
(PG)		10	-2	8/10
Spiroxyine hydrochloride hemihydrate	500	300	-3	7,7
(HOH)		100	-2	10/10
18-Benzylidene-17-hydroxy-yohimbane	250	200	>+19	1/10
(PG)		100	-2	9/10
Monothioglutarimide	100	50	>+17	3/9
(PG)		25	+3	10/10
2-Iminopiperidine hydrochloride	150	50	+1	8, 10
(HOH)		25	-5	10, 10
N-(2-Nitroisobutyl)piperidine	200	100	-1	10/10
(PG)		50	+3	15/10

1-Piperidine ethanethiol, monohydrochloride (HOII)	75	50 25	0 -1	10/10 10/10
1-Methyl-p-aminoethylthioazocyclohexane (HOH)	250	200 100	-4 0	10/10 10/10
1-{(2-Mercaptoethylthio)methyl}-4-methyl piperazine, polymer (PG)	200	100 50	5 1	9/10 10/10
4-Piperidinobenzaldehyde thiosemicarbazone (PG)	75	25 10	+1 -5	4/10 10/10
1-Phenyl-1-cyclopentyl-3-piperidino-1- propanol hydrochloride (HOH)	250	100 50	-3 -2	10/10 10/10
Isocinchomeronic acid (pyridine 2,5- dicarboxylic acid) (HOH + NaHCO3)	>1000	1000 500	-6 0	10/10 10/10
2-Mercaptopyridine (PG)	250	260 100	-5 -5	10/10 10/10
Zinc derivative of 3-pyridinethiol (PG)	150	100 50	2 +4	10/10 8/10
Pyridoxal hydrochloride (HOH)	400	300 200	-1 -2	9/10 9/10
Thioisonicotinamide (PG)	250	200 100	+1 -1	10/10 10/10
Thioisonicotinamide-1-oxide (HOH)	750	500 300	0	10/10 10/10
Isonicotinaldehyde thiosemicarbazone (PG)	150	100 50	-2 -1	10/10 10/10
Nicotinaldehyde thiosemicarbazone hydrochloride (HOH)	150	100 50	-3 -3	10/10 10/10
Methyl-2-pyridyl ketone thiosemicarbazone (PG)	5	2 1	+2 -1	10/10 10/10
Methyl-3-pyridyl ketone thiosemicarbazone (PG)	25	10 5	-1 0	10/10 10/10
Nicotinylthiosemicarbazide hydrochloride (HOH)	750	500 300	+1 0	10/10 10/10
Trimethylamine isonicotinamide (PG)	450	300 200	+2 +5	10/10 10/10

Isonicotinamidoguanylmercaptoacetic acid hydrochloride (HOH)	750	500 300	+1	10/10 10/10
Benzyl-4-benzylpyridinium chloride (HOH)	75	50 25	-3 0	10/10 10/10
Quinoline (synthetic) (PG)	200	100	+3 +9	7/11 6 10
Isoquinoline (PG)	150	100 50	-4 -1	10/10 10/10
6-Quinolinecarboxylic acid (HOH + NaHCO ₃)	>1000	1000	2 2	10/10 8 9
3-Hydroxycinchoninic acid (PG)	250	200 100	1 0	9/10 10 10
3-Hydrazinoquinoline dihydrochloride (HOH)	250	200 100	> +18 > +22	5 10 3 9
6-Methoxy-8-aminoquinoline (PG)	25	10 5	+2 4	10 10 10/10
2-Hydroxy-3-n-butyl-9,10-dimethoxy-1, 2,3,4,5,7-hex: hydro-benzo(a)quinolizine hydrochloride (HOK)	150	100 50	-3 1	10-10 10/10
6-Heptyl-4-quinosinol.1-oxide (PG)	450	300 200	-3 +1	10·10 10·10
2-Methyl-1,4-nar nthoquinone-1-thiosemi- carbazone (PG)	75	50 25	-2 -2	10, 10 10/10
7-Chloro-4-[(2-diethyl)andinoethylamino] quinoline-1-oxide (PC)	150	109	+1	10/10 9/10
7-Chloro-4-[3-(1-pyrrolidinyl) propylamino] quinoline,1-oxide (PG)	150	100	0 + 2	1e 1e 1e 1e
Cinchophen (PG)	200	100 50	-3 -45	10,10 10/10
1.7-Bis(N-tetrabydroisoquinolyi)heptane dibydrochloride (HOM)	250	50 25	-2 .:3	10 13 9, 10
1,10-Bis(N-tetrahydroisoquinolyl)decane dihydrochloride (PG)	159	50 25	+1 -2	10 10 10 10

2,3,3a,5,6,11,12,12a-Octahydro-8 hydroxy- 1H-isoquino(2,1a)(1)pyridinium bromide (HOH)	75	25 10	-2 -1	10/10 7/7
7-[2-Hydroxy-3-(N-2-hydroxyethyl-N-methylamino)-propyl]-1,3-dimethylxan-thinepyridine-3-carboxylate (Complamex) (HOH)	>1000	1000 500 250 50	0 +3 -2 -4	10/10 10/10 10/10 10/10

OXAZOLES AND OXAZINES

	Toxicity		Radiation studies	studies	
Compound and vehicle used for toxicity and radiation tests	Approx. LD ₅₀ (mg./kg.)	Dose (mg./kg.)	Change in ST ₅₀ (days)	Mortality at 30 days	
3-(2-Hydroxyethy!)-2-oxazolidinone (HOH)	750	500 300	-1 -1	10/16 10/10	
2-[2-(4-Morpholinyl)ether]-2-thiopseudourea, dihydrochloride (HOH)	40	25 10	0 -3	10 10 10/10	
N-[2-Amidinothio)ethyl]-4-morpholine- carboxamide, monohydrochloride (HOH)	750	500 300	+-4 +-2	6/10 10/10	
4- { [(2-Diethylaminoethyl)thio]methyl }-4- methylmorpholinium-p-toluenesulfo::ate metho-p-toluenesulfonate (HOH)	100	50 25	-2 0	10/10 9/10	
4-[2-(Diethylaminomethylthio)ethyl]-4- methylmorpholinium-p-toluenesulfonate metho-p-toluenesulfonate (HOH)	50	25 10	-1 0	16 10 10/10	
2-Imin-9-4-methyl-5-phenyloxazoline (PG)	10	5 1	+3 -4	10/10 9 10	
4-Morpholinobenzaldehyde thiosemicarbazone (PG)	75	50 25	+5 -5	9/10 10/10	
n-Heptyl ester of 4-(γ-morpholine propexy) benzoic acid hydrochloride (HOH)	500	300 200	7 -3	10, 10 19/10	

THIAZOLES AND THIAZINES

	Toxicity		Radiation studies	Radiation studies		
Compound and vehicle used for toxicity and radiation tests	Approx. LD ₅₀ (mg./kg.)	Dose (mg./kg.)	Change in ST ₅₀ (days)	Mortality at 30 days		
2-Amino-2-thiazoline (PG)	150	100 50	-1 -5	10/10 10/10		
2,4-Triazolidinedione (PG)	750	300 200	-1 +2	10/10 10′'0		
2,4-Dimethylthiazoie (PG)	250	200 100	0	9/10 10/10		
Thiazolidine-4-carboxylic acid (HOH)	150	100 50	+7	10/10 7/10		
Penicillamine (HOH)	350	300 100	+1 +1	8/10 10/10		
6-Aminopenicillanıc acid (PG)	>1000	500 300	+1 -1	10/10 10/10		
5-(p-Chlorobenzylidene)-2-thiothiazolidine- 2,1-dione (PG)	75	50 25	+6 -8	9/10 10/10		
2-Thioureido-4-(p-nitrophenyl)thiazole (PG)	150	100 50	0 -8	7/10 10/10		
5-(p-Dimethylaminobenzoylidene)rhodanine (PG)	150	100 50	+2 3	9/10 9/10		
5-Benzylidene-2-phenylimino-4-thiazoiidinone (PG)	75	50 25	+1 -2	8/10 10/10		
5-(p-Acetamidobenzylidene)-3-(p-acetamido- benzoylideneamino)rhodanine (PG)	100	50 25	+1 -4	6/10 8, 10		
6-Ethoxy-2-mercaptobenzothiazole (PG)	250	200 100	2 +2	10/10 8/10		
5-Chloro-2-mercaptobena thiazole (PG)	150	100 50	+2 -5	10 10 10/10		
2-(Dimethylaminomethylthio)benzothiazole (HOH)	150	100 50	+1 -6	10/10 10/10		
Ethyl-3-methyl-1-oxo-5-piperidino-2,a- thiazolidine acetate (PG)	400	400 260	- 1 0	9 10 9/10		
2-Amino-1,5-diphenylthiazole (PG)	200	200 100	-7 -4	10/10 10/19		

2,5-Bis(4-pyridyl)-1,3,4-thiadiazole	100	100	-4	10 10
(PG)		50	0	10 10
5-Benzylidenerhodanine	75	50	-2	10 10
(PG)		25	-2	10 10
3-Amino-5-benzylidenerhodanine	100	50	+1 1	10/10
(PG)		25	+2	10/10
5-Benzylidene-3-benzylideneaminorhodanine (PG)	256	200 100	+1	8 10 9/10
5-Benzylidene-3-salicylideneaminorhodanine (PG)	75	50 40 25 15	$ \begin{array}{c c} -1 \\ -3 \\ >+22 \\ 0 \end{array} $	10/10 10/10 4/10 10/10
2-(p-Methoxybenzylidenehydrazino)-4-oxo- 5-th:azolidineacetic acid (HOH + NaHCO ₃)	>1000	500 300	+3 +2	10/10 10/10
2-[(p-Acetamidobenzylidene)hydrazino]- 4-oxe-5-thiazolidineacetic acid (HOH + NaHCO3)	100	50 25	-1 +2	10/10 10/10
5,5'-Methylidynedirhodanine with triethyl- amine (PG)	150	100 50	-3 -5	10/10 10/10
2,2-Dimethyl-3-thiomorpholone	400	250	-3	10 10
(PG)		100	+2	8/10
2,2-Diethyl-3-thiamorpholone	250	200	-1	8/10
(PG)		100	-2	16/10
2-M-thyl-1,5-benzothiazepin-4-(5H)-one	400	300	+2	10/10
(PG)		200	+3	10/10
4-Methyl-1,5-benzothiazepin-2-(3H)-one	400	300	-1	6/9
(PG)		200	+ i	10/10
2,3-Dihydro-1,5-benzothiazepin-4-(5H)-one	750	500	0	9/10
(PG)		300	+3	10/10
2,3-Dihydro-7-methyl-1,5-benzothiazepin- 4-(5H)-one,1,1-dioxide +PG)	400	30° 200	+7 +2	7/10 10/10
2,3,4,5-Tetrahydro-1,5-benzothiazepin, monohydrochioride (HOH)	400	300 200	+19 +3	4 8 10 10
Thionine	400	300	-3	10/10
(HOH)		200	-3	10/10
Methylene blue chloride	150	100	-5	10/10
(HOH)		50	-2	10/10
(2-Chlorophenothiazino) propylbiguanide hydrochloride (HOH)	100	50 25	-4 -8	10/10 10/10

DIAZOLES AND DIAZINES

	Toxicity		Radiation studies	
Compound and vehicle used for toxicity and rediation tests	Approx. LD ₅₀ (mg./kg.)	Cose (mg./kg.)	Change in ST ₅₀ (days)	Mortality at 30 days
1-Isopropyl-2-(2-furyl)-4,4-dimethyl- imidazolidine (PG)	250	200 100	-3 0	10/19 10/10
1,2-Diphenyl-4,4-dimethylimidazəlidine (PG)	150	100 50	-1 +1	10/10 10/10
1-(1,1-Dimethyl-2-hydroxyethyl)-4,4- dimethyl-2-imidazolidinethione (PG)	250	200 100	0	10/10 10/10
1-Isopropyl-4,4-dimethyl-2-imidazolidine- thione (PG)	150	100 50	0 +5	8/10 10/10
1-Butyl-4,4-dimethyl-2-imidazolidinethione (PG)	150	100 50	-5 +1	10/10 10/10
1-(1,1,3,3-Tetramethylbutyl)-4,4-dimethyl- 2-imidazolidinethione (PG)	100	50 25	5 +1	10/19 30/10
1-Octadecyl-4,4-dimethyl-2-imidezolidine- thione (PG)	250	290 100	-1 -2	10/10 10/10
1-Phenyl-4,4-dimethyl-2-imidazolidinethione (PG)	200	100 50	0 +1	10/10 10/10
2-[(p-Nitrobenzyl)thio]-2-imidazoline, monohydrobromide (HOH)	50	25 10	-1 +1	10/16 10/10
2-[(m-Chlorobenzyl)thio]-2-imidazoline, monohydrobromide (HOH)	75	25 10	+1 +1	10/10 10/10
2,2- { [(Tetrachloro-p-phenylene)methylene] thio } -di-2-imidazoline, dihydrochloride (HOH)	150	100 50	-1 0	6/7 10/10
2-[2-(Diethylamino)ethyl]-5-methyl-211. (1)benzothiopyrano-4,3,2-imidazole (PG)	200	100 50	-5 -2	10/16 10/10
6,7-Dihydro-3-methyl-1-5H-imidazo(2,1- β)thiazolium chloride (HOH)	75	50 25	-2 -1	10/10 10/10

2-Amino-1,3,4-thiadiazole, monohydrochloride	250	200	-3	10 10
(HOH)		100	+2	10/10
5-Amino-1,3,4-thiadiazole-2-thiol	350	200	4 1	8/10
(HOH)		100	-2	10/10
2-Amino-5-mercapto-1,3,4-thiadiazole	250	200	4-2	5/10
(PG)		100	-2	10/10
2,5-Dimercapto-1,3,4-thiadiazole	750	200	-5	10 10
(HOH)		100	-3	10/10
1,3,4-Thiadiazole-2,5-dithiol	150	100	-2	10/10
(PG)		50	+3	10/10
2,2'-Dithio-bis'5-amino-1,3,4-thiadiazole) (PG)	150	100 50	2 3	10/10 9/10
2-Amino-5-(p-aminophenylmercapto)-1,3,4- thiadiazole (PG)	250	260 100	-1 -3	8/10 10 10
5-Anilino-1,3,4-t'dadiazole-2-thiol (PG)	250	200 100	-1 0	8/10 10 10
2-(4-Pyridyl)-5-phenyl-1,3,4-chiadiazole (PG)	150	100 50	- 2	10/10 10 10
2-Methyl-1,3.4-thiadiazole-5-phc::ylhydrazine	75	50	-2	16/10
(PG)		25	-2	10 10
2-Pheryl-1.3,4 thiadiazole-5-sulfonamide	250	200	1	10 10
(PG)		100	0	9/10
3-Allyl-2-thiohydantoin	250	290	6	10/10
(HOH)		100	+ i	10/10
3-(2-Aminoethyl)-2-thiohydantoin (HOH)	400	300 200	-1 -3	10/10
3-Phenyl-2-thionydantoin	75	25	+1	9/13
(PG)		10	5	10/10
3-Methyl-5-phenyl-5-(2-thienyl)hydantoin (PG)	150	100 50	-2 +3	10/10
5-Cyclohexylethyl-5-(2-thienyl)hydantein	150	100	-5	10/10
(PG)		50	0	8/10
3-Phenyl-5-(p-hydroxybenzyl)-2- t'110hydantoin (PG)	150	100 50	-6 -7	10 10 10, 10
5-Cyclchexylbutyl-5-(2-thienyl)hydantoin	200	100	- 5	10, 10
(PG)		50	4	10/10

1-Isonicotinyl-3,5-dimethylpyrazole (PG)	250	200 100	2 1	10/10 10/10
3,5-Dioxo-1,2-diphenyl-4-n-butylpyrazolidene (Butazolidin) (PG)	150	100 50	-5 0	9/10 9/10
3,5-Dioxo-1-phenyl-2-p-hydroxy-phenyl- 4-n-butylpyrazolidene (Oxyphenbutazone) (PG)	150	100 50	2 0	10/10 9/10
N-[(2,3-Dimethyl-5-oxo-1-phenyl)-3- pyrazolin-4-yl]-anthranilic acid (HOH + NaHCO ₃)	100	50 25	+3 +2	8/10 10/10
1,2-Diphenyl-4-methylthioethyl-3,5- pyrazolidinedione (PG)	200	100 50	-1 >+15	10/10 9/10
1,2-Diphenyl-4-(2'-phenylsulfinethyl)- 3,5-pyrazolidinedione (Sulfinpyrazone) (PG)	150	100 50	0 -2	8/10 9/10
Quinoxaline (PG)	250	200 100	>+18 >+22	3/10 1/10
2,3 Quinoxalinediol (PG)	200	100 50	-7 -2	7/10 7/10
2,3-Quinoxalinedithiol (PG)	100	50 25	-5 +3	10/10 9/10
2,3-Di-(p,p'-dimethoxystyryl)quinoxaline (PG)	250	100 50	-4 -3	10/10 10/10
4-Quinazolinol, 3-oxide (PG)	250	200 100	+2 -1	10/10 10/10
4-Quinazolinethiol (PG)	750	500 300	>+17 >+19	4/10 4/10
6-Chloro-4-quinazolinethiol (PG)	>1000	1000 500	-2 +2	10/10 10/10
3-Propyl-4-(3H)-quinazolinethione (PG)	200	100 50	0 -1	10/10 10/10
3,4-Dihydro-4-phenyl-2(1H)-quinazoline- thione (PG)	75	50 25	0 +3	10/10 10/10
3-Benzyl-2,3-dihydro-2,2-dimethyl-4(1H)- quinazolinethione (PG)	450	300 200	-2 +4	10/10 10/10

8-(p-Acetylphenyl)-6-chloro-2-thio- 2,4-(1H,3H)-quinazolinedione (PG)	250	200 100	-3 +2	10/10 10/10
7-Chloro-4-[(3-diethylaminopropyl)amino] quinoline-1-oxide (PG)	150	100 50	+1 +3	9/10 10/10
2-Dimethylaminopyrazine hydrochloride (HOH)	200	100 50	-3 -2	10/10 9/9
6-Amino-3-pyridazinethiol (PG)	400	300 100	+1 +2	10/10 8/10
Dithiothymine (PG)	200	100 50	0 +1	9/10 10/10
6-Aminouracil (sodium salt) (HOH)	> 1000	500 300	-2 +1	10/10 10/10
2-Ethylthio-4-amino-6-oxypyrimidine (PG)	200	100 50	+2	6/10 7/10
5-Bromuracil (HOH + NaHCO ₃)	> 1000	1000 500	-6 -2	10/10 10/10
5-Carbethoxy-2-thiouracil (PG)	250	200 100	0 +1	10/10 5/10
4'-(1,4-Dihydro-2-mercapto-4,4,6-trimethyl- 1-pyrimidinyl) acetophenone (PG)	75	50 25	-2 0	7/10 10/10
1,4-Dihydro-1-(o-mercaptophenyl)-4,4,6- trimethyl-2-pyrimidinethiol (PG)	400	250 100	-3 +2	10/10 8/10
1-Methylpiperazine (PG)	150	100 50	+1 -2	10/10 10/10
1-m-Methylbenzylpiperazine (PG)	100	50 25	+1 -1	10/10 10/10
N-Benzyl N'-benzoylpiperazine (HOH)	400	100 50	-5 -1	10/10 10/10
1-(3,4-Dichlorophenyl)-4-methoxyeropyl piperazine sulfate (HOH)	250	200 100	-7 -2	10/10 10/10
1,4-Piperazinediacetic acid, dihydrate (PG)	>1000	500 300	-4 -3	10/10 10/10
2-Pyridylethylpiperazine (PG)	150	100 25	-6 0	10/10 10/10

a-Ethyl-3-methyl-6-oxo-1(6H)-pyridazine acetic acid hydrazide (PG)	625	500 300	>+19 +3	4/10 5/10
1-[(Ethylthio)methyl]-1,4-dimethylpipera- zinium di-p-toluenesulfonate, polymer (HOH)	7.5	5 1	0 -1	10/10 10/10
Thiocyanic acid, 4-hydroxy-a-3-(4-methyl- 1-piperazinyl)-3,5-xylyl ester (PG)	75	50 25	+1 +1	10/10 10/10
1-(2-Methoxyphenyl)-4-thiofuran (PG)	400	300 100	-4 -2	10/10 10/10
1,4-Dimethyl-1,4-bis[2-(morpholinomethyl- thio)ethyl]-piperazinium di-p-toluene- sulfonate bis(metho-p-toluene) sulfonate (HOH)	40	25 10	+1 +3	10/10 10/10
1,1,4-Trimethyl-4 { [2-(4-methyl-1-piper- azinyl) ethylthio]methyl } piperazinium di-p-toluenesulfonate bis-(metho-p- toluene) sulfonate (HOH)	250	100 50	0 -3	9/10 10/10
6-Chloro-o-methyl-2H-1,2,4-benzothiadiazin- 7-sulfohydroxamic acid, 1,1-dioxide hemihydrate (PG)	400	300 100	-5 -7	10/10 10/10
7-Chloro-2-(cyclopropylamino)-5-phenyl- 3H-1,4-benzodiazepine-4-oxide (PG)	150	100 50	-1 -1	12/15 7/10

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TRIÁZOLES AND DIOXANES

	Toxicity		Radiation studies	
Compound and vehicle used for toxicity and radiation tests	Approx. LD ₅₀ (mg./kg.)	Dose (mg./kg.)	Change in ST ₅₀ (days)	Mortality at 30 days
S-Trithiane (Corn oil)	250	200 100	-2 -5	10/10 10/10
5-Amino-1H-1,2,4-triazole 3-carboxylic acid, sodium salt (HOH)	>1000	1000 500	0 -1	10/10 10/10
3-Mercapto-S-hydroxy-1,2,4-triazino-6- carboxylic acid (PG)	250	200 100	-3 -1	10/10 10/10
2,6-Diaminopurine sulfate (HOH + NaHCO ₃)	250	200 100	-1 0	10/10 10/10
2-Thio-6-oxypurine (HOH + NaHCO ₃)	625	500 300	-4 0	10/10 10/10
2,8-Dithio-6-oxypurine (HOH + NaHCO ₃)	400	300 100	.4	10/10 10/10
p-(2-Amino-6-hydroxy-8-purinylazo)- benzenesulfonic acid (HOH)	>1000	1000 500	+2 -6	10/10 10/10
2,6-Bis-(diethylolamine)-4,8-dipiperidino- pyrimido-(5,4-d) (PG)	150	100 50	-1 -1	10/10 10/10
1-Phenyl-5-mercaptotetrazole (PG)	250	200 50	-11 -1	10/10 10/10
Hypoxanthine (HOH + NaHCO ₃)	750	500 300	-1 -2	10/10 10/10
8-Azaguanine (HOH + NaHCO ₃)	>1000	1000 500	-8 -2	10/10 10/10
1-Methyl-2-mercapto-4,7-dihydroxy-1, 3,5,6-tetrazaindene (PG)	750	500 300	0 -7	8/10 10/10
1-Phenyl-2-mercapto-4,7-dihydroxy- 1,3,5,6-tetrazaindene (PG)	250	200 100	+1 -2	8/10 9/10
7-Theophylline acetamide (1,2,3,6-Tetrahydro- 1,3-dimethyl-2,6-dio: .purine-7-acetamide) (PG)	750	500 300	-1 -2	9/10 10/10

Ethyl-7-theophylline acetate (Ethyl-1,2,3,6- tetrahydro-1,3-dimethyl-2,6-dioxopurine- 7-acetate) (PG)	>1000	1000 500	+2 +1	7/10 7/10
8-(2-Dimethylaminoethoxy)theophylline (1,3-Dimethyl-8-(2-dimethylamino- ethoxy) xanthine) (PG)	750	500 300	-3 >+19	9/10 4/10
7,7'-Trimethylene-bis { 8-[bis(2-hydroxy- ethyl)amino]theophylline } (PG)	1000	1000 500	>+19	3/10 9/10
1,2-Cyclobutanedicarboguanamine (PG)	75	50 25	0 -2	10/10 10/10
1,2-Cyclobutanedicarboguanamine phosphate (HOH)	400	300 100	0 -1	10/10 10/10
1-Methyl-5-mercapto-1,2,3,4-tetrazole (PG)	400	300 260	-6 -11	10/10 10/10
2-Phenyl-1,5-benzothiazepin-4(5H)-one (PG)	400	300 200	-2 +7	7/10 5/10
2-(Benzylmethylamino)-7-chloro-5-phenyl- 3H-1,4-benzodíazepine-4-oxide (PG)	300	200 100	+3 -2	7/10 10/10
5-Methyl-7-phenyl-3H-1,2-dithiepin-3-thione (PG)	250	200 100	+3 +1	7/10 8/9
7-Chloro-1-methyl-5-phenyl-1H ·1,4-pen- zodiazepine-2(3H)-thione (PG)	250	200 50	01	6/10 10/10
5-Nitro-5-methyl-1,3-dioxane (PG)	150	100 50	+2 +3	10/10 10/10
2-Methyl-3-ethanol benzodioxane (HOH)	400	300 100	-3 +1	10/10 10/10

MISCELLANEOUS

	Toxicity		Radiation studies		
Compound and vehicle used for toxicity and radiation tests	Approx. LD ₅₀ (mg./kg.)	Dose (mg./kg.)	Change in ST ₅₀ (days)	Mortality at 30 days	
Calcium chloride	>200	200	+1	10/10	
(HOH)		100	-2	10/10	
Sodium chlorate	>1000	1000	-1	10/10	
(HOH)		500	+1	10/10	
Sodium borate, tetra	>1000	1000	-1	10/10	
(HOH)		500	+1	10/10	
Sodium nitrite		125	+6	9/10	
(HOH)		100	0	8/10	
2-Nitropropane	75	50	-3	10/10	
(PG)		25	+2	10/10	
2,3-Dibromopropane	75	50	-4	10/10	
(PG)		25	-3	10/10	
2-Bromopentane	150	100	-7	10/10	
(PG)		50	-3	10/10	
1,3-Dibromopropane	750	500	-1	10/19	
(HOH)		200	0	10/10	
Naphthalene	150	100	-2	10/10	
(PG)		50	-4	10/10	
a-(Methoxymethyl)naphthalene	200	100	-6	9/10	
(PG)		50	-3	10/10	
Calcium flavonate	625	500	-4	10/10	
(HOH)		300	+3	10/10	
Vitamin B ₁₂ with intrinsic factor concentrate (HOH)	>1000	1000 500	-4 0	10/10 10/10	
Corn oil	>50000	50000	0	10/10	
Olive oil	> 50000	50000	-1	10/10	
Petrolatum (liquid)	>50000	50000	0	10/10	
Safflower oil	> 50000	1 cc.	+2	10/10	
Sesame oil	> 50000	50000	-1	9/10	

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13. ABSTRACT

This report summarizes the results obtained with 617 compounds tested for their radioprotective activity in adult male mice irradiated with a controldemonstrated LD₉₉₊ of 800 R (250 kvp) x-rays. A compound was considered to exhibit radioprotective activity if it (1) permitted any of the treated mice to survive for 30 days after the otherwise lethal whole-body x-irradiation or (2) increased the median survival time of treated animals by 5 days or more beyond the median survival time of the untreated control mice (9 1 3 days).

Of the 617 compounds tested, 245 successfully passed one or both of the stated specifications. Additionally, data are offered to allow comparisons of chemically related groups for structure-activity relationships, and to indicate the types of structures which offer the greatest promise as a source of more effective and less toxic radioprotective agents.

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